Topics in Primary Care Medicine

The Evaluation and Management of Acute Diarrhea

SUSAN W. TOLLE, MD, *and* DIANE L. ELLIOT, MD, *Portland*

"Topics in Primary Care Medicine" presents articles on common diagnostic or therapeutic problems encountered in primary care practice. Physicians interested in contributing to the series are encouraged to contact the series' editors.

BERNARD LO, MD
STEPHEN J. McPHEE, MD
Series' Editors

About 10% of all ambulatory visits are for acute diarrheal illnesses. Understanding their epidemiology and clinical features allows appropriate use of laboratory evaluation and rational patient management. Our discussion is limited to acute diarrheal illnesses of less than three weeks' duration.

Clinical Presentation

The differential diagnosis of acute diarrhea can be divided into the clinical syndromes of noninflammatory and inflammatory types of diarrhea. Noninflammatory secretory diarrhea is associated with cramping, bloating, periumbilical pain and large-volume watery stools. Fever and constitutional symptoms are minimal or absent. In contrast, inflammatory diarrhea or dysentery is associated with mucosal invasion and commonly accompanied by fever, other constitutional symptoms, lower abdominal pain and tenesmus. Stools are usually of small volume and often bloody or mucoid.

Causes of noninflammatory diarrhea include rotavirus, Norwalk agent, enterotoxigenic *Escherichia coli, Vibrio cholerae* and *Giardia lamblia,* as well as bacterial toxins associated with food poisoning. These organisms or toxins do not invade the mucosa but induce a secretory watery diarrhea, thus hematochezia and fecal leukocytes are typically absent. In the United States, Norwalk virus and other presumed viral agents are the most common causes of noninflammatory diarrhea in adults and produce a self-limited illness with explosive diarrhea lasting 24 to 48 hours. Rotavirus infection predominates in infants and young children and produces severe watery diarrhea of five to eight days' duration.

Travel history, recent food and drug ingestion and sexual practices are important when considering causes of diarrheas. In 25% to 50% of travelers to Mexico diarrhea develops, 70% of which is due to enterotoxigenic *E coli.* Less frequent causes of traveler's diarrhea include *Salmonella, Shigella, G lamblia* and *Entamoeba histolytica.* Although the profound secretory diarrhea caused by *V cholerae* is primarily a problem in developing nations, infection is endemic in the bayous of Louisiana and sporadic cases have been reported from these areas. Wilderness travel increases the risk of giardiasis, which is enzootic in some wild mammals, resulting in contamination of streams. Rates of giardiasis are increasing in the United States, and travel is not necessary to acquire the infection. Symptoms include bloating, cramping, periumbilical pain and foul-smelling watery stools, developing two weeks following exposure.

Foodborne diarrhea can be noninflammatory, due to bacterial toxins, or inflammatory following the ingestion of invasive pathogens. Food poisoning should be suspected when outbreaks of diarrhea occur in companions. A specific bacterial toxin may be suggested by the clinical setting. Staphylococcal toxin causes the abrupt onset of nausea and vomiting two to seven hours following the consumption of contaminated meat, poultry, cream-filled pastries or mixed salads. Abdominal cramping and diarrhea also occur. Toxicity with *Clostridium*

(Tolle SW, Elliot DL: The evaluation and management of acute diarrhea [Topics in Primary Care Medicine]. West J Med 1984 Feb; 140:293-297.)

From the Division of General Internal Medicine, Department of Medicine, The Oregon Health Sciences University, Portland.
Supported in part by US Dept of Health and Human Services Training Grant No. 1-1-D28-PE10051-04.
Reprint requests to Susan W. Tolle, MD, Division of General Internal Medicine, Department of Medicine, The Oregon Health Sciences University, 3181 SW Sam Jackson Park Road, Portland, OR 97201.

perfringens requires replication of the organism, thus the onset of symptoms is delayed for 8 to 14 hours after consumption of contaminated meats. Vomiting is infrequent, and the main features include abdominal cramps and watery diarrhea that persist for 24 hours. A less common foodborne diarrhea is due to *Bacillus cereus* toxin, which can produce the pattern seen with either staphylococcal or *C perfringens* toxicity.

Inflammatory diarrhea caused by *Salmonella, Shigella, Campylobacter jejuni, Vibrio parahaemolyticus, Yersinia enterocolitica* and invasive *E coli* can also be acquired through the ingestion of contaminated food or water. Nontyphoidal *Salmonella* is the most common infectious agent identified with cases of foodborne diarrhea. Poultry, eggs and raw milk are frequently contaminated food sources. Large bacterial inoculums are required to produce illness, which is due to both bowel invasion and an enterotoxin-induced secretory diarrhea. Malaise and watery diarrhea begin 6 to 24 hours following ingestion. Fever and dysentery may also occur.

Shigellosis, often a biphasic illness, exhibits early features of a noninflammatory diarrhea characterized by the passage of voluminous watery stools. However, high fever often suggests an invasive diarrhea before the development of dysentery. This shift to an inflammatory diarrheal pattern usually occurs by the second day. *Shigella* is highly infectious, and person-to-person transmission is common. While dysentery with bloody diarrhea has traditionally suggested shigellosis, in the western United States, *Campylobacter* is now identified as often as *Shigella* in this setting.

Campylobacter-induced illness causes abdominal pain, diarrhea, nausea, vomiting, malaise and fever. Patients may have grossly bloody stools. Unlike *Shigella,* transmission of *Campylobacter* between adults has not been observed. The usual incubation period is two to seven days after the ingestion of contaminated materials. Most cases are sporadic, but infection has been associated with ingestion of raw milk and contact with sick pets.

Contaminated raw milk has also been implicated in outbreaks of diarrhea due to *Y enterocolitica.* Symptoms range from stools containing blood and mucus to profuse watery diarrhea. The frequency of *Yersinia* as a cause of acute diarrhea is unknown, as identification of the organism requires special culture techniques with enrichment at low temperatures.

V parahaemolyticus, a marine organism, is a major cause of outbreaks of food poisoning associated with the ingestion of contaminated seafood and shellfish. The incubation period is 4 to 96 hours. Symptoms are usually noninflammatory and include abdominal cramps, nausea, vomiting and watery diarrhea.

Medication may precipitate diarrheas. Noninflammatory diarrhea may be caused by the ingestion of stimulant laxatives or sorbitol in artificial sweeteners. Diarrhea associated with recent antibiotic use suggests the possibility of antibiotic-associated colitis. Symptoms usually include noninflammatory watery diarrhea that appears at any time up to six weeks following antibiotic therapy. In severe cases, dysentery with high fever occurs. Virtually any antibiotic can cause this syndrome. Currently, the three most commonly implicated agents are cephalosporins, ampicillin and clindamycin. Antibiotic use facilitates the overgrowth of *Clostridium difficile,* which produces a toxin damaging to the colonic mucosa.

Certain sexual practices predispose persons to selected infectious diarrheal states. Homosexual men are at increased risk for infections with *Shigella, Campylobacter, G lamblia, E histolytica, Chlamydia trachomatis, Herpes simplex* and *Neisseria gonorrhoeae.* The last is usually asymptomatic but can appear as proctitis or dysentery.

Other diseases, such as ulcerative colitis and ischemic colitis, can also present as acute diarrhea.

Laboratory Evaluation

A variety of laboratory tests may assist in determining the cause of a patient's diarrhea. The usefulness of fecal leukocyte determination, stool culture and proctoscopy varies with the clinical setting. The presence of fecal leukocytes suggests colonic mucosal invasion. A thin layer of feces or mucus is applied to a slide, mixed with one drop of Loeffler's methylene blue, sealed with cover slide and examined microscopically for leukocytes. The presence of more than five polymorphonuclear leukocytes per high power field is considered positive. Polymorphonuclear leukocytes are specific for colonic inflammation and suggest infection due to *Shigella, Campylobacter* and invasive *E coli,* antibiotic-associated colitis, ulcerative colitis and ischemic colitis. This test is not sensitive enough, however, to detect all forms of diarrhea associated with colonic invasion. For example, in one study fecal leukocytes were found in only 69% of *Shigella* infections, and similar results have been reported for *Campylobacter* infections.

Fecal leukocytes are rarely identified with noninflammatory diarrhea due to toxins, viruses, enterotoxigenic *E coli* and *G lamblia.* In antibiotic-associated colitis, leukocytes are few or absent when the process is limited but are common in diffuse disease. Likewise, *E histolytica, Salmonella, Y enterocolitica* and *V parahaemolyticus* infections produce variable findings, and the presence of leukocytes depends on the degree of colonic invasion.

Because most acute diarrheal illnesses are self-limited and caused by viruses, stool bacterial cultures should be used judiciously. Cultures are reserved primarily for the following cases: patients who have occult blood or are positive for fecal leukocytes, febrile patients (temperature above 38.3°C [101°F]), those requiring admission to hospital, food handlers and those who have diarrhea for more than one week. Identification of *Campylobacter* using selective culture medium is possible in most laboratories and should be requested

in all patients cultured. Cultures of rectal specimens for gonorrhea should be added when evaluating diarrhea in homosexual men. Follow-up stool cultures are rarely indicated except for patients with rectal gonorrhea and food handlers.

Most cases of bacillary dysentery have a similar sigmoidoscopic appearance. However, the procedure is useful in the diagnosis of antibiotic-associated colitis, amebic colitis and ulcerative colitis. When these diagnoses are suspected, sigmoidoscopic examination should be done. In addition, it is indicated for patients with culture-negative dysentery or diarrhea persisting for more than seven to ten days. Antibiotic-associated colitis is diagnosed when yellow-gray plaques (2 to 10 mm) are seen. If these findings are absent, the diagnosis can be confirmed by rectal biopsy, assessment of stool *C difficile* toxin titer or anaerobic culture of the organism.

The localized colonic ulcerations of amebiasis can be identified and suctioned or scraped during proctoscopy. Amebas tend to adhere to cotton swabs, and specimens should be obtained directly. Untrained observers may not distinguish amebas from leukocytes, and a skilled parasitologist is needed to confirm the diagnosis. Serologic examinations, with gel diffusion precipitin or indirect hemagglutination tests, are positive in 85% to 90% of patients with amebic colitis.

Sigmoidoscopy in cases of ulcerative colitis shows a diffusely erythematous and friable rectal mucosa, and evaluation for bacterial pathogens and amebas will be negative. About 10% of patients with ulcerative colitis have acute diarrhea as their initial symptom.

Examination for parasites should be carried out when undiagnosed diarrhea persists for more than a week or when travel history or sexual preference suggests increased risk for amebiasis or giardiasis. A total of three stool specimens, promptly delivered to a laboratory or collected with preservative, is optimal. Identification of ameba may be delayed for weeks by a prior barium examination, enemas, laxatives and certain antibiotics.

When diarrhea persists for two weeks, strong consideration should be given to giardiasis. Trophozoites are reliably identified in a stool specimen only during the first few days of acute illness. Small bowel aspiration with biopsy at the duodenojejunal junction may be required to recover the organism. The Enterotest, a gelatin capsule on a string, has been reported by some investigators to be as effective as duodenal intubation in confirming infection.

Barium enema examination is generally not part of the evaluation of acute diarrhea. Its major diagnostic use is in ischemic colitis, which occasionally appears as acute diarrhea. In cases of acute inflammatory diarrhea, the procedure will be irritating and carries risks of megacolon and perforation.

Therapy

The general management of acute diarrhea depends on a patient's age, underlying medical conditions and state of hydration. Therapy for noninflammatory diarrhea is directed at rehydration. Mild dehydration can be corrected with fruit juices or caffeine-free soft drinks. The absorption of sodium and water in the small intestine is more effective in the presence of glucose. Thus, more severe dehydration should be treated with a balanced glucose and electrolyte oral rehydration solution (Table 1) or an equivalent commercial preparation. Intravenous hydration is occasionally required. Beverages containing ethanol or caffeine increase intestinal motility and should be avoided. Transient lactose intolerance is commonly associated with acute diarrhea, and milk and dairy products should also be avoided.

TABLE 1.—*Oral Rehydration Solution*

One liter (1 qt*) of water containing
3.5 grams (½ tsp) sodium chloride (table salt)
2.5 grams (½ tsp) sodium bicarbonate (baking soda)
1.5 grams (¼ tsp) potassium chloride (salt substitute)
20 grams (4 tbsp) glucose (sugar)

*Approximations for home use

Symptomatic treatments of noninflammatory diarrhea can be grouped into three categories. The most controversial are the antiperistaltic agents: paregoric, tincture of opium, diphenoxylate hydrochloride with atropine sulfate (Lomotil) or loperamide hydrochloride (Imodium). These drugs decrease stool volume and relieve cramps but may impair the clearance of infectious agents and toxins. Antiperistaltics may prolong the duration of shigellosis and increase the risk of intestinal perforation in cases of amebiasis. If these drugs are used, stool cultures should be taken, and patients should be advised against their use when fever or symptoms suggesting inflammatory diarrhea are present.

A second group of medicines are the inhibitors of intestinal secretion, of which bismuth subsalicylate (Pepto-Bismol) is the prototype. When taken after the onset of diarrhea (60 ml every half hour for eight doses), abdominal cramps are relieved and bowel movements reduced in both enterotoxigenic *E coli* and viral diarrhea. These large volumes (240 ml) can be inconvenient, however, and have a salicylate content equal to 2.6 grams of aspirin.

The final group of symptomatic agents are the absorbents such as kaolin (Kaopectate) or charcoal. Although they are reported to absorb toxins and may alter the consistency of the stool, they do not diminish symptoms, number of bowel movements or fluid and electrolyte losses.

Antibiotic therapy may be indicated when specific pathogens are identified (Table 2). In general, noninflammatory diarrhea is self-limited, antibiotics are rarely required and volume repletion is the therapy of choice. However, antibiotics are generally used in the treatment of noninflammatory diarrhea due to *G lamblia* and *V cholerae*. In giardiasis, a cure rate of 95% is attributable to the use of quinacrine hydrochloride, and metronidazole is an alternate form of therapy. In the

uncommon but profound secretory diarrhea of cholera, tetracycline is the antibiotic of choice.

The prophylaxis of traveler's diarrhea and the treatment of diarrhea due to enterotoxigenic *E coli* are controversial. Although antibiotic treatment can reduce the duration of symptoms, illness is usually self-limited, and therapy may be associated with side effects and facilitate the development of antibiotic resistance. We advise travelers to avoid buffet-style meals, to drink bottled or carbonated beverages and to carry a bottle of Pepto-Bismol and a five-day course of trimethoprim-sulfamethoxazole. If diarrhea develops, early treatment with Pepto-Bismol and antibiotics will usually result in a prompt resolution of symptoms.

Prophylactic treatment is reserved for medically compromised patients. Trimethoprim, 160 mg, plus sulfamethoxazole, 800 mg, taken as a single daily dose or doxycycline, 100 mg taken twice a day, is effective in preventing most forms of traveler's diarrhea. Diarrhea developing during prophylaxis or unresponsive to treatment suggests campylobacteriosis, giardiasis, amebiasis or antibiotic-associated diarrhea and requires medical evaluation.

Inflammatory diarrhea often requires antibiotic therapy. Confirmed rectal gonorrhea always requires treatment. Recommended therapies are procaine penicillin or ampicillin, and spectinomycin dihydrochloride pentahydrate is used for penicillin-allergic patients. Tetracycline is specifically not recommended because its use for rectal gonorrhea results in a 15% failure rate.

Shigella sps are often resistant to ampicillin, and trimethoprim-sulfamethoxazole are now the antibiotics of choice. Although in vitro resistance to tetracycline is common, single high-dose therapy is often effective. Many patients with shigellosis improve rapidly before culture results are available and do not require treatment to facilitate recovery. Because the duration of shedding of this highly infectious organism can be shortened with antibiotic therapy, we choose to treat all symptomatic patients who have confirmed shigellosis.

The diarrhea associated with *C jejuni* is largely self-limited, and antibiotic treatment begun late in the course may not alter the resolution of symptoms. However, we recommend treatment of severe or protracted disease. Most strains are susceptible to erythromycin, and it is the treatment of choice. Likewise, *Yersinia*-associated colonic diarrhea is usually mild, self-limited and requires no treatment. Patients who have severe infections respond well to tetracyclines, but no studies have proved them superior to other antibiotics.

Antibiotic therapy is typically withheld in nontyphoidal *Salmonella,* as its use promotes the development of the carrier state. However, antibiotics are given for patients with bacteremia, those at high risk for bacteremia (infants, elderly, immunocompromised and sickle cell patients) and those with prosthetic devices as foci for the development of infection. When drug susceptibility is unknown, chloramphenicol is the agent of choice. Ampicillin or trimethoprim-sulfamethoxazole should be used in susceptible isolates.

Amebic dysentery requires treatment, but antiprotozoan therapy is controversial. Metronidazole remains the drug of choice for amebic dysentery in adults, with a cure rate of 90%. Some authors recommend combining metronidazole with iodoquinol. An alternate therapy for amebic dysentery is dehydroemetine dihydrochloride

TABLE 2.—*Pathogen-Specific Antibiotic Therapy in Acute Diarrhea*

Pathogen	*Treatment of Choice**	*Alternative Therapy*
Giardia lamblia	Quinacrine hydrochloride, 100 mg every 8 hr for 7 d	Metronidazole, 250 mg, every 8 hr for 7 d
Vibrio cholerae	Tetracycline, 250 mg every 6 hr for 5 d	Trimethoprim, 80 mg, plus sulfamethoxazole, 400 mg, 1 tab every 12 hr for 5 d
Rectal gonorrhea	Procaine penicillin G, 4.8 million units intramuscularly, plus 1.0 grams of probenecid	Ampicillin, 3.5 grams, plus 1.0 grams of probenecid, orally, or spectinomycin dihydrochloride pentahydrate, 4 grams intramuscularly
Shigella sps	Trimethoprim, 160 mg, plus sulfamethoxazole, 800 mg, 1 tab every 12 hr for 5 d	Ampicillin, 500 mg, every 6 hr for 5 d or tetracycline, 2.5 grams as a single dose
Campylobacter jejuni†	Erythromycin, 500 mg, every 6 hr for 7 d	Tetracycline, 250 mg, every 6 hr for 7 d or clindamycin, 300 mg, every 6 hr for 7 d
Yersinia enterocolitica†	Tetracycline, 250 mg, every 6 hr for 7 d	Trimethoprim, 160 mg, plus sulfamethoxazole, 800 mg, 1 tab every 12 hr for 7 d
Nontyphoidal *Salmonella* sps‡	Ampicillin, 1 gram intravenously every 4 hr for 14 d, or trimethoprim, 160 mg, plus sulfamethoxazole, 800 mg, 1 tab every 12 hr for 14 d	Chloramphenicol, 1 gram intravenously every 6 hr for 2 wk
Entamoeba histolytica	Metronidazole, 750 mg, every 8 hr for 5 to 10 d, plus iodoquinol, 650 mg, every 8 hr for 21 d	Dehydroemetine dihydrochloride, 90 mg a day intramuscularly or subcutaneously for 10 d
Pseudomembranous colitis†	Discontinue incriminated antibiotic; vancomycin, 125 mg, every 6 hr for 10 d	Bacitracin, 25,000 units, every 6 hr for 10 d

*Adult dosages, and all antibiotics are given by mouth unless otherwise stated.
†Antibiotics reserved for severe illness
‡Antibiotics not indicated except in special circumstances

given in conjunction with iodoquinol. Dehydroemetine is held as a second-line drug due to cardiac and neurologic toxicity.

Mild antibiotic-associated diarrhea usually resolves following the withdrawal of the offending antibiotic. However, antibiotic-associated colitis due to *C difficile* usually requires eradication of the organism. Vancomycin given by mouth is currently the treatment of choice. Relapse due to recrudescence of sporulate organisms occurs in up to 20% of patients and requires retreatment with vancomycin. Its high cost, bad taste and high relapse rate have led investigators to explore therapeutic alternatives. Orally given bacitracin and metronidazole are being evaluated for therapeutic efficacy. Controversy exists regarding the use of resins that bind the *C difficile* toxin. Recent studies suggest that the efficacy of cholestyramine resin or colestipol hydrochloride is limited only to mild illness. They should not be used in combination with oral vancomycin because they tend to bind with the antibiotic.

GENERAL REFERENCES

Baker RW, Peppercorn MA: Gastrointestinal ailments of homosexual men. Medicine (Baltimore) 1982 Nov; 61:390-405

Fekety R: Recent advances in management of bacterial diarrhea. Rev Infect Dis 1983 Mar-Apr; 5:246-257

Pickering LK, DuPont HL, Olarte J, et al: Fecal leukocytes in enteric infection. Am J Clin Pathol 1977 Nov; 68:562-565

Plotkin GR, Kluge RM, Waldman RH: Gastroenteritis: Etiology, pathophysiology and clinical manifestations. Medicine (Baltimore) 1979 Jan; 58:95-114

Satterwhite TK, DuPont HL: Infectious diarrhea in office practice. Med Clin North Am 1983 Jan; 67:203-220